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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,853	07/08/2003	Henry Chiu	P1973R1	5148
9157 7590 02/23/2007 GENENTECH, INC. 1 DNA WAY SOUTH SAN FRANCISCO, CA 94080			EXAMINER SPECTOR, LORRAINE	
			ART UNIT	PAPER NUMBER
			1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary**Application No.**

10/614,853

Applicant(s)

CHIU ET AL.

Examiner

Lorraine Spector, Ph.D.

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 1-21 and 23-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22, 29 and 30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-30 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 July 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date. <u>01-26-04</u> | 6) <input type="checkbox"/> Other: _____ |

10/614853

DETAILED ACTION

Election/Restrictions

Applicants have elected invention IX, claims 22, 29 and 30 without traverse. Applicants allege that the elected claims are 20, 28 and 29. This is incorrect. As pointed out in the restriction requirement, at page 1, line 1, the claims as originally submitted were not consecutively numbered, and were renumbered under 37 CFR §1.126, as numbers 11, 29 and 30 had been omitted (the originally submitted claims ended with claim 33). Thus, the claims under consideration, as correctly numbered by the examiner, are 22, 29 and 30. Applicants are advised that a correctly numbered copy of the claims, as renumbered by the Examiner, appears in PAIR with a document date of 11/7/2006.

The claims are drawn to a method of diagnosing an immune related disease in a mammal, comprising detecting the level of expression of a gene encoding PRO71061, corresponding to the nucleic acid of SEQ ID NO: 1, the protein product of SEQ ID NO: 2, and also identified as DNA304494.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

It is noted that the specification refers to the protein of SEQ ID NO: 2 as PRO71061. However, it is noted that, while applicant may be their own lexicographer, the protein is also variously known as PRO5801 and IL-17RH1 in U.S. Patent Number 6,579,520, IL17RLP in U.S. Patent Number 6,849,719, and as IL-17BR in a publication by Shi et al., JBC 275(25):19167-19176, 2000, all cited herewith by the Examiner.

Drawings

The drawings/figures are objected to because tables and sequence listings included in the specification must not be duplicated in the drawings. See 37 C.F.R. §1.58(a) and §1.83. Figures

1-28 (all of the figures) consist of nothing more than amino acid and nucleic acid sequences. Any additional information therein (start codons, etc.) may be properly designated as part of the computer-readable sequence listing. Accordingly, the figures are entirely duplicative of the sequence listing. Applicants are advised that upon issuance of a patent, the complete text of the sequence listing submitted in compliance with 37 C.F.R. §§1.821-1.825 will be published as part of the patent. Applicants should amend the specification to delete any Figures which consist only of nucleic acid or protein sequences which have been submitted in their entirety in computer readable format (i.e. as SEQ ID NO:'s) and should further amend the specification accordingly to reflect the replacement of the Figure by the appropriate SEQ ID NO:.

Appropriate correction is required.

Claim Objections

Claims 22, 29 and 30 are objected to for encompassing non-elected inventions. Each and every PRO listed constitutes a patentably distinct invention, there being no genus claim, and there being no structural relationship between the various PRO genes. Accordingly, the claims should be amended to read only upon the elected invention.

Correction is required.

Rejections under 35 USC §112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22, 29 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite as the metes and bounds of "PRO71061" are not clear. The specification provides a single nucleic acid, SEQ ID NO: 1, that is said to *be* PRO71061, and states that innumerable variants derivatives, and homologs are also envisioned as being PRO71061. Further, as stated above, the same gene/protein has been reported by different groups under different names, including one group with two common inventors and the same

assignee as this application. Accordingly, it is not clear what meaning is to be given to "PRO71061", and accordingly, what the metes and bounds of the claims are.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention in a manner commensurate in scope with the claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to methods of diagnosing immune disorders. Claim 22 encompasses diagnosis of *any* "immune related" disease in a mammal by assaying for *either* increased or decreased expression of PRO71061. Claim 29 is limited to diagnosis of "a B-cell mediated immune response", and Claim 30 to "a B-cell mediated disease". The specification itself does not provide adequate written description or enablement of such methods, as no specific immune disorders are disclosed as being so diagnosable. Further, as the claims allow for either detection of *increased or decreased* gene expression, and it is not believable that both would be associated with a single disorder, the specification appears merely to proffer, based upon the finding that PRO71061 is expressed at a higher level in activated B cells than in a "universal normal" control, an invitation to experiment to determine what types of conditions

could be diagnosed by the claimed methods, and whether one would be looking for increased or decreased expression in such conditions. Such an invitation to experiment is not enabling.

Example 1 merely compares expression levels in activated B cells to a “universal normal control” comprising “non-cancerous, human tissues, including liver, kidney and lung”, which would not be accepted in the art as being a valid comparison to establish the PRO71061 gene as being upregulated in inflammatory disease, a necessary correlation for the enablement of the pending claims.

However, the Examiner is aware that applicants are not required to teach that which is known in the prior art, and as evidenced by the art rejections below, it was known that the gene in question was diagnostic of at least some immune disorders. Specifically, the prior art teaches the following:

Shi et al., JBC 275(25):19167-19176, 2000, teach that IL-17BR, which is the same gene as PRO71061, is a receptor for a variant of IL-17, which Shi et al. designate IL-17B. They teach that the receptor is normally expressed in kidney, pancreas, liver, brain and intestines, and in only a few of many cell lines tested. While liver and kidney are included in the “universal normal” control used by applicants, it is noted that no expression was found by Shi in lung, the third tissue listed; further, the universal normal control is merely described as “including” liver, lung and kidney tissues; it is not clear what else it might ‘include’. Nonetheless, given Shi’s results, one could reasonably conclude *nothing* about there being a higher level of expression in activated B cells compared to the “universal normal” control used by applicants, other than that the gene *is* expressed by activated B cells; one cannot conclude that it is expressed *more or less* than in non-activated B cells based on applicants disclosure, nor whether it is expressed *more or less* than in any single individual tissue type. What Shi et al. report, however, is that the gene is “drastically up-regulated during intestinal inflammation elicited by indomethacin treatment in rats”; see the abstract, and page 19176. It is notable that Shi et al. did *not* find expression in DSS-induced colitis, another model of inflammatory bowel disease. Shi goes on at page 19176 to discuss further correlation of indomethacin-induced inflammation with Crohn’s disease. Therefore, one can conclude that it is *reasonably* predictable, but not certain, that upregulation of PRO71061 would be diagnostic of Crohn’s, but no other disease, based upon Shi’s results.

U.S. Patent Number 6,849,719, by Shi et al., discloses IL17RLP, which as noted above, is the same as PRO71061. At column 9, Shi states “It has been discovered the IL17RLP is

expressed not only in adult pulmonary tissue, but also in Crohn's Disease tissue...." and goes on to specifically teach the use of nucleic acids, protein and antibodies for use in diagnostic methods "for a number of disorders of the above tissues or cells, particularly of the immune system, significantly higher or lower levels of IL17RLP gene expression may be detected..." The claimed invention is clearly stated at lines 55-62 or column 9. Further, Crohn's disease is a B-cell mediated disease, in the sense that B cells are involved in the disease process. Claims are drawn to antibodies and methods for detecting IL17RLP.

Finally, with respect to the prior art, U.S. Patent Number 6,579,520, which has two common inventors with the current application, discloses PRO5801, also referred to therein as IL-17RH1, which is identical to PRO71061. At columns 123-124, it is stated that PRO5801 is "highly expressed in the kidney, significant expression in liver and peripheral organs such as colon, small intestine, prostate, testis, pancreas and uterus", and "not expressed in heart, bone marrow, spleen and placenta." At column 128 it is established that PRO5801 is a receptor for IL-17E, but not IL-17 or IL-17C (terminology as used therein). At column 129, it is disclosed that IL-17E is a proinflammatory cytokine. It is further stated that "a key consideration in understanding the function of the different members of the expanding IL-17 cytokine family will be the expression patterns and regulation of the cognate receptors." At columns 133-134, it is shown that IL-17E is upregulated in inflammation. However, there is no showing or suggestion that the *receptor*, designated PRO5801 therein and PRO71061 herein, is so upregulated. There is, in fact, no showing of any differential expression of the receptor in any disease state, nor suggestion that receptor expression levels would be diagnostic.

Art Unit: 1647

Accordingly, although it seems clear that Crohn's disease may be diagnosed by assaying expression levels of PRO71061, it is not predictable what other "immune related" diseases may be so diagnosed, nor whether the expression of PRO71061, which is the receptor for an IL-17-related cytokine would be increased or decreased in a particular disease, and in which tissues. Accordingly, in view of the state of the art as discussed herein, the amount of experimentation required to fully develop the claimed invention in a manner commensurate in scope with the claims, and the complete absence of any working example demonstrating diagnosis of any immune related condition using the claimed method, enablement is not commensurate in scope with the claims.

Rejections over Prior Art

The instant application claims priority to provisional application 60/397,485, filed 7/8/2002. As the references applied herein predate that filing date, no determination has been made on the merits of the priority claim.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 22, 29 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 6,849,719, by Shi et al. The filing date of the Shi patent is 3/2/2001. Shi discloses IL17RLP, which as noted above, is the same as PRO71061. At column 9, Shi states "It has been discovered the IL17RLP is expressed not only in adult pulmonary tissue, but also in Crohn's Disease tissue...." and goes on to specifically teach the use of nucleic acids, protein and antibodies for use in diagnostic methods "for a number of disorders of the above tissues or cells,

Art Unit: 1647

particularly of the immune system, significantly higher or lower levels of IL17RLP gene expression may be detected...” The instantly claimed invention is clearly stated at lines 55-62 or column 9. Further, Crohn’s disease is a B-cell mediated disease, in the sense that B cells are involved in the disease process. Claims are drawn to antibodies and methods for detecting IL17RLP. Accordingly, the claims are clearly anticipated by Shi et al.

Claims 22, 29 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication Number 2005/0181372, by Shi et al. This application is a divisional of the patent discussed above, and claims “A method of diagnosing a disease or disorder which comprises:

- contacting a biological sample from a test subject with the antibody of claim 20;

- (a) assaying the level of IL17RLP polypeptide in the biological sample; and

- (b) comparing the level of IL17RLP polypeptide in the biological sample with a standard level of IL17RLP polypeptide;

whereby an increase or decrease in the level of IL17RLP polypeptide compared to the standard level of IL17RLP polypeptide is indicative of a disease or disorder.

Accordingly, the claims are clearly anticipated by Shi et al.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1647

Claims 22, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi et al., JBC 275(25):19167-19176, 2000.

As discussed above, Shi et al. teach that IL-17BR, which is the same gene as PRO71061, is a receptor for a variant of IL-17, which Shi et al. designate IL-17B. They teach that the receptor is “drastically up-regulated during intestinal inflammation elicited by indomethacin treatment in rats”; see the abstract, and page 19176. It is notable that Shi et al. did *not* find expression in DSS-induced colitis, another model of inflammatory bowel disease. Shi goes on at page 19176 to discuss further correlation of indomethacin-induced inflammation with Crohn’s disease. Therefore, one can conclude that it is *reasonably* predictable, but not certain, that upregulation of PRO71061 would be diagnostic of Crohn’s, but no other disease, based upon Shi’s results. Accordingly, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to use expression levels of IL-17BR, aka PRO71061, as a diagnostic for Crohn’s disease, in view of Shi’s explicit teachings that the receptor is “drastically up-regulated” in a recognized model of Crohn’s disease. Accordingly, the invention as claimed is *prima facie* obvious over the Shi JBC disclosure.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. at telephone number 571-272-0893.

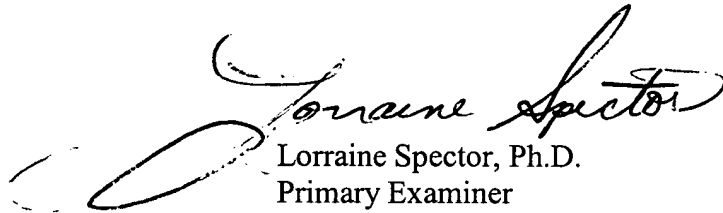
If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Ms. Brenda Brumback, at telephone number 571-272-0961.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to **571-273-8300**. Faxed draft or informal communications with the examiner should be directed to **571-273-0893**.

Art Unit: 1647

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read "Lorraine Spector". The signature is fluid and cursive, with a large initial "L" and "S".

Lorraine Spector, Ph.D.
Primary Examiner